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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/704,362	11/01/2000	Kalyanaraman Ramnarayan	24737-1906B	4748

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[REDACTED] EXAMINER

BRUSCA, JOHN S

ART UNIT	PAPER NUMBER
1631	R

DATE MAILED: 08/13/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)
	09/704,362	RAMNARAYAN ET AL.
	Examiner John S Brusca	Art Unit 1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 03 June 2002.
- 2a) This action is **FINAL**.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 23 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 23 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

#### Attachment(s)

- 1) Notice of References Cited (PTO-892)  
 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)  
 3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6,8,12.
- 4) Interview Summary (PTO-413) Paper No(s) \_\_\_\_\_.  
 5) Notice of Informal Patent Application (PTO-152)  
 6) Other:

## **DETAILED ACTION**

### ***Information Disclosure Statement***

1. The information disclosure statements filed 21 February 2001 and 19 March 2002 fail to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. The missing references have not been considered.
2. The information disclosure statements filed 21 February 2001 and 19 March 2002 fail to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent listed that is not in the English language. It has been placed in the application file, but the information referred to therein has not been considered.

### ***Election/Restrictions***

3. Applicant's election without traverse of Group 3 in Paper No. 11 is acknowledged. The nonelected claims have been cancelled by the applicants in the amendment filed 03 June 2002.

### ***Inventorship***

4. In view of the papers filed 03 June 2002, the inventorship in this nonprovisional application has been changed by the deletion of P. Patrick Hess.

The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of the file jacket and PTO PALM data to reflect the inventorship as corrected.

### ***Claim Rejections - 35 USC § 112***

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5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 23 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation." These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) In order to practice the claimed invention one of skill in the art must predict the clinical response of a patient to a drug by determination of a structure of a polypeptide from a polymorphic site by use of sequence data. For the reasons discussed below, there would be an unpredictable amount of experimentation required to practice the claimed invention.

b) The specification does not present specific guidance to determine the structure of a polypeptide from sequence data.

c) The specification does not present a working model of determination of the structure of a polypeptide from sequence data.

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d) The nature of the invention, prediction of the clinical response of a patient to a drug by determination of a structure of a polypeptide from a polymorphic site by use of sequence data, is complex.

e) Sternberg et al. and Koehl et al. review a meeting held in late 1998 known as CASP3. CASP3 was designed to test contemporary polypeptide structure prediction methods in a blind contest. Various classes of structure determination methods were used to predict structures that were recently experimentally determined but whose structure was not available to the participants of CASP3 until after submission of their structure predictions. Thus, the accuracy of the predictions could be predicted by comparison to the corresponding polypeptide structures. Koehl et al. and Sternberg et al. show that there were three types of algorithms employed. The first were used on sequences that had a significant degree of similarity to known polypeptide structures (comparative modeling). The second type of algorithm was used on sequences with folding domains with a significant degree of similarity to known polypeptide domains (fold recognition). The third type of algorithm relied either partially or not at all on structural predictions based on similarity to known polypeptides (ab initio prediction). Both figure 2 of Sternberg et al. and table 1 of Koehl et al. show that for sequences with "new folds", i.e., sequences without significant similarity to known polypeptide structures, the ab initio algorithms had a relatively poor ability to predict structure, and predicted the positions of only about half of the residues of the sequence. Sternberg et al. and Koehl et al. demonstrate that at the effective filing date of the instant application, knowledge of known polypeptide structures with similarity to a polypeptide sequence of interest was of great benefit in predicting the structure of the polypeptide sequence of interest. Sternberg et al. and Koehl et al. further show that at the

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effective filing date of the instant application, the best ab initio methods were unable to accurately predict structures of complete polypeptides in the absence of knowledge of structures of polypeptides with similarity to the polypeptide sequence of interest. It is apparent from instant claim 23 that the claimed method requires an ab initio method to accurately predict the structure of a polymorphic polypeptide sequence in the absence of additional structural information.

- f) The skill of those in the art of polypeptide structure and modeling is high.
- g) Both Sternberg et al. and Koehl et al. show that ab initio methods of structure prediction from polypeptide sequence information alone is not predicted to result in an accurate structure of a complete polypeptide.
- h) The claims are broad in that they are drawn to modeling polypeptide structures in the absence of information other than sequence information.

The skilled practitioner would first turn to the instant application for guidance in practicing the claimed method. However, the instant application does not provide specific guidance to predict structures of polypeptides in the absence of information other than sequence information. The skilled practitioner would next turn to the prior art, but the prior art does not provide adequate guidance to practice the claimed invention as discussed above. Finally, said practitioner would turn to trial and error experimentation to practice the claimed invention. Such represents undue experimentation.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 23 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 23 is indefinite for recitation of the phrase "derived based on" in page 47, line 27. It is not clear what the phrase means in relation to the rest of the claim.

Claim 23 recites the limitation "the structural variant-drug complex models" in page 48, lines 1-2. There is insufficient antecedent basis for this limitation in the claim.

Claim 23 is indefinite for recitation of the phrase "a molecular graphics interface for 3-D molecular structure visualization; functionality for protein sequence and structural analysis; database searching tools" because those recited elements cannot be part of a database as required by the claim.

Claim 23 is indefinite for recitation of the phrase "based on" in page 48, line 9 because it is not clear what the phrase means in relation to the rest of the claim.

Claim 23 recites the limitation "the same gene associated with a polymorphism in a patient" in page 48, lines 9-10. There is insufficient antecedent basis for this limitation in the claim.

Claim 23 is indefinite for recitation of the phrase "screening/comparing" in page 48, line 13 because it is not clear if both or only one of the processes are part of the claim.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Brusca whose telephone number is 703 308-4231. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on 703 308-4025. The fax phone numbers for the organization where this application or proceeding is assigned are 703 746-5137 for regular communications and 703 746-5137 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308-0196.

*John S. Brusca*  
John S. Brusca  
Primary Examiner  
Art Unit 1631

jsb  
August 9, 2002